REMARKS

Claims 1 and 31-75 are in the application.

No claims are amended herein.

Entry of this Reply, reexamination and reconsideration of the application are respectfully requested in light of the Declaration under 37 CFR 1.132 of Gerald E. McDonnell submitted with the previous Reply and the following remarks.

Declaration Under 37 CFR 1.132 of Gerald E. McDonnell

Applicants submitted with the previous Reply to Office Action the Declaration under 37 CFR 1.132 of Gerald E. McDonnell ("the Declaration"), one of the inventors of the present application. Applicants respectfully submit that the Examiner failed to properly credit certain facts submitted in the Declaration and failed to appreciate the import of those facts, and relied instead on the Burdon prior art that was less relevant and probative, and relied to an unjustifiable extent on the allegedly contrary statements by Burdon.

The Declaration includes a brief discussion of the need for a prion surrogate for use in testing prion decontamination compositions and processes, and includes data showing that IFDO is an effective and valid surrogate for prions in such testing. Applicants respectfully submit that the Declaration fully responds to the Examiner's concerns and overcomes any possible contention that the present application lacks an enabling disclosure with respect to effectiveness of the claimed process against prions, when using IFDO as a surrogate.

Response to Examiner's Comments in Office Action

Applicants respectfully submit that, when the Declaration is properly understood and the data in the application as filed are considered, the presently claimed invention not only distinguishes over the prior art, but patentably so distinguishes and the presently pending claims therefore should be allowed. Applicants respond as follows to the Examiner's comments in the Office Action, in which the Declaration was found insufficient and the application was contended to lack evidence of synergy in the presently claimed invention when compared to the prior art.

1. Evidence Contended to be Not Commensurate With Claim Scope.

In the Office Action to which this Reply responds, the Examiner contended that the scope of the Declaration is not commensurate with the scope of the claims. Applicants respectfully submit that this basis for distinguishing the strength of the facts in the Declaration is based on a misunderstanding of the purpose of the data in the Declaration. To wit, the Declaration was intended to show that, for a wide variety of prion decontamination methods, IFDO is a valid surrogate for prions, when *in vitro* IFDO results are compared to results of *in vivo* animal studies using actual prions.

The data in the Declaration, as discussed below, show a 1:1 correlation between test results from *in vitro* IFDO and from *in vivo* animal studies using actual prions.

The Declaration was submitted for the above-noted purpose, not for the purpose of showing that the present invention is superior to prior art methods and in fact provides a synergistic effect when compared to the closest prior art, which is an earlier version of LpH®. The superiority and the synergistic effect are shown by the data in the specification itself, as discussed in more detail below.

To the extent that the Examiner contends that the data shown in paragraph (9) of the Declaration is insufficient in that it presents comparison data for only a limited number of decontamination processes, Applicants respectfully submit that it would be well nigh impossible for Applicants to provide evidence to show that IFDO is a valid surrogate for prions using every possible form of decontamination. To satisfy such a demand, Applicants would have to test IFDO against actual prions using every possible type of sterilization process, and would have to do so using prions in *in vivo* animal studies which, as established by Dr. McDonnell's Declaration, would take years to obtain results. This is simply not a reasonable demand, since it establishes an impossible-to-meet standard.

Accordingly, Applicants submit that the evidence already submitted clearly shows that the presently claimed invention is fully enabled, that IFDO is a valid surrogate for prions, and that, when considered with the data shown in the application itself, that the presently claimed invention fully distinguishes over the prior art and the claims are in condition for allowance.

2. Evidence Contended to Not Show Equal Effectiveness.

In the Office Action to which this Reply responds, the Examiner contended that the evidence in the Declaration at one specific set of conditions shows that conditions that are effective against IFDO are not equally effective against prions, and thereby distinguished and refused to accept the evidence as proof of the validity of IFDO as surrogate for prions. Applicants respectfully submit that this alleged rebuttal of the facts in the Declaration is incorrect and is not in accordance with all the facts clearly set forth in the Declaration, for the following reasons.

In paragraph (5) of the Declaration, the Declarant stated:

> (5) *In vitro* Western blots have been used to detect the presence/absence of the prion protein PrPSc as detected by its resistance to protease treatment and the use of an antibody directed against the PrP protein. It has been published that Western blots are not good predicting methods for inactivation of prions (e.g. Fichet et al., 2004. Lancet **364**: 521-526.) (Emphasis added.)

Thus, the Declaration clearly stated the fact that the *in vitro* Western blot method is not good for predicting inactivation of prions. That is, it would be expected by the skilled person that Western blot tests would be imperfect in reflecting true results. This statement has not been rebutted. For this reason, the fact that Western blot test results were not consistent with *in vivo* animal studies with prions and with *in vitro* IFDO studies does not support the Examiner's refusal of the evidence.

For the Examiner's convenience, a copy of the above-referenced Lancet article is submitted herewith. On page 526, the article states: "In any case, our data show that the assessment of decontaminant efficacy should not rely solely on western-blot analyses."

In paragraph (6) of the Declaration, the Declarant stated:

> (6) *In vivo* animal models have been used to test the presence/absence of prion infection in a solution or when contaminated on a surface. The most widely used method uses the prion scrapie strain 263k in sensitive mice or hamsters. The typical incubation time is at least 1 year and could be as long as 3 years. (Emphasis added.)

Any person of ordinary skill in the art would readily recognize that while *in vivo* animal tests provide a "gold standard" for the presence or absence of prions, since, as stated in the Declaration, the animal models take a very long time to provide results, such tests are not practical for routine use in determining whether an object is or is not contaminated with prions. Obviously, people cannot be expected to wait around for 1-3 years to determine whether an object, such as a surgical instrument, is or is not contaminated by prions, prior to use or handling of the object. This provides another strong reason for and evidence of the need for a surrogate for prions for purposes of testing prior disinfection agents and processes.

The other primary reason for working with a surrogate was provided in paragraph (3) of the Declaration, when Dr. McDonnell stated that due to the nature of prions, it is necessary to employ a surrogate whenever possible, to avoid the possibility of infection to personnel in the laboratory environment in which the testing is carried out, or others who might inadvertently be exposed to the prions. As used in the present application, and in the other patents cited by Applicants in a previous Reply, IFDO is a valid and useful surrogate for such testing.

In paragraph (9) of the Declaration, test results were provided. In a first column, *in vitro* Western blot data was provided for prions, in a second column *in vivo* animal study data was provided for prions, and in a third column, *in vitro* IFDO study data was presented. The table is reproduced below for easy reference:

Inactivation Method	**Prion Studies**		**IFDO Studies** (*in vitro*)
	Western Blot (*in vitro*)	Animal Tests (*in vivo*)	
1N NaOH (20°C, 1 hour)	+	+	+

Steam sterilization (134°C, 18 mins)	+	+[1]	+[1]
Alkaline formulation (Hamo100)			
(1.6%, 43°C, 15 mins)	+	+	+
(0.8%, 43°C, 7.5 mins)	+	+	+
(0.2%, 25°C, 5 mins)	+	+/–	+/–
Hydrogen Peroxide Gas			
(1.5mg/L, 25°C, 3 hours, atmospheric pressure)	–	+	+
(2mg/L, 30°C, 3 pulses at 5 mins/pulse, under vacuum)	+/–[2]	+	+
(6mg/L, 50°C, 4 pulses at 7.5 mins/pulse, under vacuum)	+/–[2]	+/–	+/–
Liquid (60% v/v, 20°C, 15 mins)	–	+/–	+/–
Environ LpH®[3] (5%, 20°C, 30 mins)	–	+	+

As clearly shown by the table, in every single instance, the results obtained in the "gold standard" *in vivo* animal study test results are exactly the same as the results obtained in the *in vitro* IFDO study results.

The *only* differences in the sets of results in the table are between the set of *in vitro* Western blot results and the other two sets of results, i.e., the *in vivo* animal tests and the *in vitro* IFDO tests, which are consistent with each other. Thus, the *only* inconsistent test results are from the less reliable, known-to-be-suspect, Western blot tests. As noted above, no one of ordinary skill in the art would have expected that the Western blot test results, which are known to be unreliable, would exactly parallel the results from the "gold standard" *in vivo* animal studies.

By the very same token, the fact that the *in vitro* IFDO studies exactly parallel the results from the "gold standard" *in vivo* animal studies can only be interpreted as proof that IFDO is in fact a valid surrogate for prions.

The Examiner's contentions to the contrary are unsupported by any evidence, are based only on the Examiner's own speculation, and are directly contradicted by the evidence presented in the Declaration. For this reason, the Examiner's continued

rejection of Applicant's claims is clearly erroneous and is without support of substantial evidence, and therefore must be withdrawn.

Applicants therefore respectfully request the Examiner to reconsider and withdraw the rejections of Applicants' claims.

3. Examiner's Inquiry As to Specification Support for Synergy.

In the Office Action to which this Reply responds, the Examiner contended that it is unclear where in the specification there is support for the "alleged" synergy. Applicants refer the Examiner to Example 1 and Table 1 at pp. 14-15 of the specification. In Example 1, an earlier version of LpH®, which is outside the scope of the present claims, is compared to Compositions I-VIII, which are within the scope of the present claims. The conventional LpH® used in this test is the same as that disclosed by Ernst and Race, as disclosed on p. 4, lines 21-26. As disclosed on p. 15, lines 5-9 (noting that line numbering is not applied to the table), a comparative study with the conventional LpH® gave a log reduction of 4.0 IFDO after treatment. In contrast, the Compositions I-VIII gave log reductions of 5.1, 4.8, 4.9, 5.2, 5.7, 4.8, 6.7 and 5.2, respectively. Noting that these are log reductions, i.e., the values are on a logarithmic scale, these results certainly show synergy.

Accordingly, Applicants respectfully submit that the specification as filed contains ample evidence of synergy of the present invention compared to the closest prior art, and for this additional reason, coupled with the above-shown validity of IFDO as a surrogate for prions, the presently claimed invention fully patentably distinguishes over the asserted combination of prior art references arrayed against the present invention in the Office Action.

Obviousness-Type Double Patenting

Regarding the provisional obviousness-type double patenting, since neither application has been allowed, the rejection is not yet ripe, and accordingly Applicants respectfully refuse to address this provisional rejection at this time. Should a terminal disclaimer become necessary, such can be filed, if appropriate, in the later-filed application.

Furthermore, Applicants respectfully submit that the claims of the present application would not have been obvious over the claims of the later-filed application upon which this obviousness-type double patenting rejection is based. For this reason, Applicants traverse the provisional obviousness-type double patenting rejection set forth in the Office Action to which this Reply is responsive.

Rejection Under 35 USC §112, First Paragraph

Claims 1 and 31-75 stand rejected as lacking enabling disclosure. Applicants respectfully traverse this rejection for at least the foregoing reasons and for the same reasons set forth in the previous Reply to Office Action, which Applicants incorporate herein by reference in support of the traverse of this rejection.

For all of the foregoing reasons, Applicants respectfully submit that the presently claimed invention is, and was at the time the present application was filed, fully enabled in accordance with 35 USC §112, 1st paragraph, and accordingly Applicants respectfully request withdrawal of this ground of rejection.

Rejections Under 35 USC §103(a)

Claims 1, 31-40, 45-52 and 55-74 stand rejected under 35 U.S.C. §103(a) as unpatentable over Prusiner (US 6720355) and Ernst and Race (Ernst et al., "Comparative analysis of scrapie agent inactivation methods," *Journal of Virological Methods*, 41 (1993) 193-202). Claims 54 and 75 stand rejected as obvious over Prusiner and Ernst and Race, and further in view of Foster, (US 7252720). Claim 53 stands rejected as obvious over Prusiner and Ernst and Race, and further in view of McDonnell (US 7001873) and/or Narayanan (US 5326789).

Applicants respectfully traverse each of the foregoing rejections for at least the reasons set forth in the previous Reply to Office Action, which are incorporated herein by reference.

The Office Action states that because the synergistic results relate only to IFDO, and since the Declaration was found inadequate, the synergy is not shown. Applicants respectfully submit that the foregoing discussion clearly shows that IFDO is a fully valid surrogate for prions, and that therefore the data contained in the application as filed do

in fact show a synergistic effect when compared to a very close prior version of LpH®, and therefore the prior art is fully distinguished.

Applicants respectfully submit that claim 1 would not have been obvious over the prior art cited by the Examiner. Claims 31-55 depend from amended claim 1 and would not have been obvious over the cited references for at least the same reasons that claim 1 would not have been over such references. Withdrawal of the rejection is believed to be warranted and is respectfully requested.

Applicants respectfully submit that claim 56 would not have been obvious over the prior art cited by the Examiner. Claims 57-75 depend from claim 56 and also would not have been obvious over the cited references for the same reasons. Withdrawal of the rejection is believed to be warranted and is respectfully requested.

Conclusion

Applicants respectfully submit that the application is in condition for allowance. A Notice of Allowance is respectfully requested.

Any additional fees required for the filing of this paper may be charged to Deposit Account No. 18-0988. In the event the Examiner would like to discuss any matter involving this application with the Applicants, he is invited to contact the undersigned attorney by telephone.

Respectfully submitted,

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